

What is claimed is:

- Sub
A1
1. A composition for the treatment of diabetic neuropathy by a method of administration selected from the group consisting of oral administration, parenteral administration and inhalation, the compositions comprising a mixture of an amount of a compound that promotes synthesis of nerve growth factor which is effective when administered in the composition to promote synthesis of nerve growth factor, an amount of an aldose reductase inhibitor which is effective when administered in the composition to inhibit aldose reductase and an effective amount of an antioxidant.
- 10 2. A composition as claimed in claim 1, wherein the compound that promotes the synthesis of nerve growth factor is selected from the group consisting of: vitamin D₃, 1(S), 3(R)-dihydroxy-20(R)-(1-ethoxy-5-ethyl-5-hydroxy-2-heptyn-1-yl)-9, 10-seco-pregna-5(Z), 7(E), 10 (19)-triene, and other vitamin D₃ derivatives which promote the synthesis of nerve growth factor, pharmaceutically acceptable salts thereof and mixtures thereof. (12)
- 15 3. A composition as claimed in claim 1, wherein the aldose reductase inhibitor is selected from the group consisting of: flavonoids, flavonoid derivatives which exhibit aldose reductase inhibiting properties, pharmaceutically acceptable salts thereof and mixtures thereof.
- 20 4. A composition as claimed in claim 3, wherein the aldose reductase inhibitor is selected from the group consisting of: ⁴⁵⁶(-)-epigallocatechin; ⁴⁵⁶(-)-epigallocatechin-gallate; 1,2,3,6-tetra-o-gallyol-β-d-glucose; 2'-o-acetylacetoside; 3,3',4-tri-o-methyl-ellagic acid; 25 6,3',4'-trihydroxy-5,7,8-trimethoxyflavone; 6-hydroxy-luteolin; 6-hydroxykaempferol-3,6-dimethyl ether; 7-o-acetyl-8-epi-loganic acid; acacetin; acetoside; acetyl trisulfate quercetin; ⁴⁵⁶amentoflavone; ⁴⁵⁶apiin; astragalin; avicularin; axillarin; baicalein; brazilin; brevifolin carboxylic acid; caryophyllene; chrysin-5,7-dihydroxyflavone; chrysoeriol; chrysosplenol; chrysosplenoside-a; chrysosplenoside-d; ⁴⁵⁶cosmosiin; ⁴⁵⁶δ-cadinene; 30 dimethylmussaenoside; diacetylirsimaritin; diosmetin; dosmetin; ellagic acid; ebinin; ethyl brevifolin carboxylate; flavocannibiside; ⁴⁵⁶flavosativaside; ⁴⁵⁶genistein; gossypetin-8-glucoside; haematoxylin; hispiduloside; ⁴¹⁵hyperin; ⁴¹⁵indole; iridine; isoliquiritigenin; isoliquiritin; ⁴⁵⁶isoquercitrin; ⁴¹⁶jionoside; juglanin; kaempferol-3-rhamnoside; kaempferol-3-neohesperidoside; kolaviron; licuraside; ⁴¹⁶linariin; linarin; lonicerin; luteolin; luetolin-7-

glucoside; luteolin-7-glucoside; luteolin-7-glucuronide; macrocarpal-a; macrocarpal-b; macrocarpal-d; macrocarpal-g; maniflavone; methy scutellarein; naringenin; naringin; nelumboside; ⁴⁵⁶ nepetin; ⁴⁵⁶ nepetrin; nerolidol; oxyyanin-a; pectolinarigenin; pectolinarin; quercetagenin; quercetin; quercimertrin; quercitrin; quercitrinyl-2'' acetate; reynoutrin; ⁴⁵⁶ rhamnetin; rhoifolin; ⁴⁵⁶ rutin; ⁴⁵⁶ scutellarein; sideritoflavone; ⁴⁵⁶ sophoricoside; ⁴⁵⁶ sorbarin; spiraeoside; ⁴⁵⁶ trifolin; ⁴⁵⁶ vitexin; ⁴⁵⁶ wogonin; pharmaceutically acceptable salts thereof, and mixtures thereof.

5. A composition as claimed in claim 3, wherein the aldose reductase inhibitor comprises at least one compound selected from the group consisting of: quercetin, quercetrin, myricetin, kaempferol and myrecetrin.

6. A composition as claimed in claim 1, wherein the antioxidant comprises at least one compound selected from the group consisting of: ascorbyl palmitate, ascorbic acid (vitamin C), vitamin A, vitamin E acetate, α -lipoic acid, especially DL- α -lipoic acid, coenzyme Q10, glutathione, catechin, glangin, ⁴⁵⁸ rutin, ⁴⁴⁰ luteolin, ⁴⁵⁶ morin, ⁴⁵⁶ fisetin, silymerin, apigenin, ginkgolides, hesperitin, cyanidin, citrin, derivatives thereof which exhibit antioxidant activity, and pharmaceutically acceptable salts thereof.

7. A composition as claimed in claim 6, wherein the antioxidant comprises a mixture of at least two different compounds.

8. A composition as claimed in claim 1, wherein the antioxidant comprises vitamin E.

9. A composition as claimed in claim 1, wherein the antioxidant comprises vitamin A.

10. A composition as claimed in claim 1, wherein the antioxidant comprises ascorbyl palmitate.

11. A composition as claimed in claim 8, wherein the antioxidant further comprises at least one compound selected from the group consisting of ascorbyl palmitate and vitamin A.

12. A composition as claimed in claim 5, wherein the compound that promotes the synthesis of nerve growth factor comprises vitamin D₃.

5 13. A composition as claimed in claim 12, wherein the antioxidant comprises at least one compound selected from the group consisting of vitamin A, vitamin E, and ascorbyl palmitate. 458

14. A composition as claimed in claim 13, wherein the antioxidant comprises vitamin A, vitamin E as mixed tocopherols and ascorbyl palmitate and the aldose reductase inhibitor comprises quercetin.

15. A composition as claimed in claim 1, further comprising an effective amount of a pharmaceutically acceptable carrier.

16. A method for the treatment of diabetic neuropathy comprises the step of administering by a method of administration selected from the group consisting of oral administration, parenteral administration and inhalation, an effective amount of a mixture which comprises an amount of a compound that promotes synthesis of nerve growth factor which is effective when administered in the composition to promote synthesis of nerve growth factor, an amount of an aldose reductase inhibitor which is effective when administered in the composition to inhibit aldose reductase and an effective amount of an antioxidant.

17. A method as claimed in claim 16, wherein the compound that promotes the synthesis of nerve growth factor is selected from the group consisting of: vitamin D₃, 1(S), 3(R)-dihydroxy-20(R)-(1-ethoxy-5-ethyl-5-hydroxy-2-heptyn-1-yl)-9, 10-seco-pregna-5(Z), 7(E), 10 (19)-triene, and other vitamin D₃ derivatives which promote the synthesis of nerve growth factor, pharmaceutically acceptable salts thereof and mixtures thereof.

18. A method as claimed in claim 17, wherein the aldose reductase inhibitor is selected from the group consisting of: flavonoids, flavonoid derivatives which exhibit

aldose reductase inhibiting properties, pharmaceutically acceptable salts thereof and mixtures thereof.

19. A method as claimed in claim 18, wherein the aldose reductase inhibitor is
5 selected from the group consisting of: (-)-epigallocatechin; (-)-epigallocatechin-gallate;
1,2,3,6-tetra-o-gallyol- β -d-glucose; 2'-o-acetylacetoside; 3,3',4-tri-o-methyl-ellagic acid;
6,3',4'-trihydroxy-5,7,8-trimethoxyflavone; 6-hydroxy-luteolin; 6-hydroxykaempferol-
3,6-dimethyl ether; 7-o-acetyl-8-epi-loganic acid; acacetin; acetoside; acetyl trisulfate
quercetin; amentoflavone; apiin; astragalin; avicularin; axillarin; baicalein; brazilin;
10 brevifolin carboxylic acid; caryophyllene; chrysin-5,7-dihydroxyflavone; chrysoeriol;
chrysosplenol; chrysosplenoside-a; chrysosplenoside-d; cosmosiin; δ -cadinene;
dimethylmussaenoside; diacetylcircimaritin; diosmetin; dosmetin; ellagic acid; ebinin;
ethyl brevifolin carboxylate; flavocannibiside; flavosativaside; genistein; gossypetin-8-
glucoside; haematoxylin; hispiduloside; hyperin; indole; iridine; isoliquiritigenin;
15 isoliquiritin; isoquercitrin; jionoside; juglanin; kaempferol-3-rhamnoside; kaempferol-3-
neohesperidoside; kolaviron; licuraside; linariin; linarin; lonicerin; luteolin; luetolin-7-
glucoside; luteolin-7-glucoside; luetolin-7-glucoronide; macrocarpal-a; macrocarpal-b;
macrocarpal-d; macrocarpal-g; maniflavone; methy scutellarein; naringenin; naringin;
nelumboside; nepetin; nepetrin; nerolidol; oxyayanin-a; pectolinarigenin; pectolinarin;
20 quercetagenin; quercetin; quercimertrin; quercitrin; quercitryl-2'' acetate; reynoutrin;
rhamnetin; rhoifolin; rutin; scutellarein; sideritoflavone; sophoricoside; sorbarin;
spiraeoside; trifolin; vitexin; wogonin; pharmaceutically acceptable salts thereof, and
mixtures thereof.

20. A method as claimed in claim 16, wherein the antioxidant comprises at least one
25 compound selected from the group consisting of: ascorbyl palmitate, ascorbic acid
(vitamin C), vitamin A, vitamin E acetate, α -lipoic acid, especially DL- α -lipoic acid,
coenzyme Q10, glutathione, catechin, glangin, rutin, luteolin, morin, fisetin, silymerin,
apigenin, ginkgolides, hesperitin, cyanidin, citrin, derivatives thereof which exhibit
30 antioxidant activity, and pharmaceutically acceptable salts thereof.

21. A method as claimed in claim 20, wherein the compound that promotes the
synthesis of nerve growth factor comprises vitamin D₃, the aldose reductase inhibitor
comprises at least one compound selected from the group consisting of: quercetin,

quercetrin, myricetin, kaempferol and myrecetrin, and the antioxidant comprises at least one compound selected from the group consisting of vitamin A, vitamin E acetate, and ascorbyl palmitate.

5 22. A method as claimed in claim 21, wherein the antioxidant comprises vitamin A, vitamin E acetate and ascorbyl palmitate and the aldose reductase inhibitor is quercetin.

23. A method as claimed in claim 16, wherein the composition further comprises an effective amount of a pharmaceutically acceptable carrier.

10

24. A method as claimed in claim 16, wherein an amount of about 11-28.6 mg/kg body weight of the patient per day of ascorbyl palmitate is employed, an amount of about 170-357.1 IU per kg body weight of the patient, per day, of vitamin A is employed, an amount of about 4-11.4 IU per kg body weight of the patient, per day, of vitamin E is
15 employed, about 13-21.4 mg/kg body weight of the patient per day of quercetin is employed, and about 6-14.3 IU per kg body weight of the patient of vitamin D₃ is employed.

25. A method as claimed in claim 16, wherein an amount of about 14.3-28.6 mg/kg
20 body weight of the patient per day of ascorbyl palmitate is employed, an amount of about 214.3-357.1 IU per kg body weight of the patient, per day, of vitamin A is employed, an amount of about 5.7-11.4 IU per kg body weight of the patient, per day, of vitamin E is employed, about 17.2-21.4 mg/kg body weight of the patient per day of quercetin is employed, and about 8-14.3 IU per kg body weight of the patient of vitamin D₃ is
25 employed.